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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/573,062	03/21/2006	Makoto Suematsu	098570203999US0	6673

7278 7590 06/21/2007

DARBY & DARBY P.C.
P.O. BOX 770
Church Street Station
New York, NY 10008-0770

EXAMINER	
LONG, SCOTT	
ART UNIT	**PAPER NUMBER**
1633	

MAIL DATE	DELIVERY MODE
06/21/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/573,062	SUEMATSU, MAKOTO	
	Examiner	Art Unit	
	Scott D. Long	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 March 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-16* is/are rejected.

7)☒ Claim(s) *13 and 16* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *3/21/2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim Status

Claims 1-16 are pending. Claims 1-16 are under current examination.

Sequence Compliance

Sequence Listing and CRF have been received and are acknowledged by examiner. A statement that the Computer Readable Form (CRF) and the Sequence Listing are identical has been submitted and is acknowledged by examiner.

Oath/Declaration

The oath or declaration, having the signatures of all inventors, received on 21 March 2006 is in compliance with 37 CFR 1.63.

Information Disclosure Statement

The Information Disclosure Statements (IDS) filed on 21 March 2006 consisting of 1 sheets are in compliance with 37 CFR 1.97. Accordingly, examiner has considered the Information Disclosure Statements.

Priority

This application claims as a 371 of PCT/JP04/14566 (filed 09/28/2004) which claims benefit of Provisional U.S. application 60/506,506 (filed 09/29/2003). The instant application has been granted the benefit date, 29 September 2003, from the application 60/506,506.

Claim Objections

Claims 13 and 16 are objected to because of the following informalities: Claims 13 and 16 contain the typographical error, "call injury," rather than "cell injury," as in claims 5 and 10. Appropriate correction is required.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-5 and 11-13 are rejected under 35 U.S.C. 102(b) as being anticipated by Sherman et al (Hepatology 1986. Vol.6; No.3: 444-449).

Claim 1 is directed to a method of analyzing organ or tissue injury, comprising the following steps of: (a) labeling an organ or a tissue with dye; (b) obtaining multiple indices involving xenobiotic metabolism and/or cell condition of said organ or tissue; and (c) analyzing the organ or tissue injury from said indices. Sherman et al. teach fluorescently labeled sodium glycocholate in liver (abstract) and utilize microscopy (page 446) to detect and analyze transport process at a cellular level (Page 446, Discussion). Sherman also teaches "different zones may function differently in the metabolism and transport of certain compounds" (page 444), satisfying the limitation regarding xenobiotic metabolism. According to the specification, page 9, lines 9-12, multiple indices includes transport across the cell membrane. Sherman et al. teach measurement of "apparent sinusoid to canaliculus transport time" and "apparent sinusoid to bile transport time" (page 445). Additionally, Sherman et al. teach, "we then tested the effect of various doses of FITC-GC on the bile flow, sinusoidal blood flow, blood pressure and heart rate" (page 445).

Claim 2 is directed to method of claim 1, wherein the organ or tissue is at least one selected from the group consisting of liver, kidney, lung, pancreas and gastrointestinal tracts. Sherman et al. teach application of their method to liver.

Claim 3 is directed the method of claim 1, where the step (b) further comprises a step of obtaining microanatomical orientation of vascular system and/or excretion pathways. Sherman et al. teach microscopy of excretion pathways, stating "observed...a reversal of the flow direction...zonal differences in excretion rate or back diffusion and transport by blood" (pages 448-449).

Claim 4 is directed to the method of claim 1, wherein the analysis is carried out visually and/or quantitatively. The method of Sherman utilized microscopic visualization by indicating "fluorescent microscopy have made possible direct visualization movement (transport) of fluorescent or fluorescently labeled molecules" (page 444).

Claim 5 is directed to the method of claim 1, wherein the cell condition is at least one selected from the group consisting of cell viability, cell injury, molecular transport, and mitochondrial function. Sherman et al. suggest obtaining indices of molecular transport. Sherman et al. teach, "we then tested the effect of various doses of FITC-GC on the bile flow, sinusoidal blood flow, blood pressure and heart rate" (page 445).

Claim 11 is directed the method of claim 2, where the step (b) further comprises a step of obtaining microanatomical orientation of vascular system and/or excretion pathways. Sherman et al. teach microscopy of excretion pathways, stating "observed...a reversal of the flow direction...zonal differences in excretion rate or back diffusion and transport by blood" (pages 448-449).

Claim 12 is directed to the method of claim 2, wherein the analysis is carried out visually and/or quantitatively. The method of Sherman utilized microscopic visualization by indicating "fluorescent microscopy have made possible direct visualization movement (transport) of fluorescent or fluorescently labeled molecules" (page 444).

Claims 13 is directed to the method of claim 2, wherein the cell condition is at least one of selected from the group consisting of cell viability, call injury, molecular transport, and mitochondrial function. Sherman et al. suggest obtaining indices of molecular transport. Sherman et al. teach, "we then tested the effect of various doses of

FITC-GC on the bile flow, sinusoidal blood flow, blood pressure and heart rate" (page 445).

Accordingly, Sherman et al. anticipated the instant claims.

Claims 1-5 and 11-13 are rejected under 35 U.S.C. 102(b) as being anticipated by Ishimura et al (EP 0687411 A1, published 20 December 1995).

Claim 1 is directed to a method of analyzing organ or tissue injury, comprising the following steps of: (a) labeling an organ or a tissue with dye; (b) obtaining multiple indices involving xenobiotic metabolism and/or cell condition of said organ or tissue; and (c) analyzing the organ or tissue injury from said indices. Ishimura et al. utilize "a rat perfused liver microcirculation monitoring system" (page 4, line 53) which utilizes a fluorescently labeled albumin to assess "injury to the cells (severity of cell necrosis) in the hepatic microcirculation" (page 5, lines 2-3). In addition, Ishimura et al. are concerned with the viability of graft preservation (page 4).

Claim 2 is directed to method of claim 1, wherein the organ or tissue is at least one selected from the group consisting of liver, kidney, lung, pancreas and gastrointestinal tracts. Ishimura et al. teach application of their method to liver.

Claim 3 is directed the method of claim 1, where the step (b) further comprises a step of obtaining microanatomical orientation of vascular system and/or excretion pathways. The method of Ishimura et al. utilizes a "technique of liver microcirculation viviperception" (page 5, line 4).

Claim 4 is directed to the method of claim 1, wherein the analysis is carried out visually and/or quantitatively. The method of Ishimura et al. utilizes microscopy to evaluate tissue damage.

Claim 5 is directed to the method of claim 1, wherein the cell condition is at least one selected from the group consisting of cell viability, cell injury, molecular transport, and mitochondrial function. Ishimura et al. assess "injury to the cells (severity of cell necrosis) in the hepatic microcirculation" (page 5, lines 2-3). In addition, Ishimura et al. are concerned with the viability of graft preservation (page 4).

Claim 11 is directed the method of claim 2, where the step (b) further comprises a step of obtaining microanatomical orientation of vascular system and/or excretion pathways. Ishimura et al. assess "injury to the cells (severity of cell necrosis) in the hepatic microcirculation" (page 5, lines 2-3). The method of Ishimura et al. utilizes a "technique of liver microcirculation viviperception" (page 5, line 4).

Claim 12 is directed to the method of claim 2, wherein the analysis is carried out visually and/or quantitatively. The method of Ishimura et al. utilizes microscopy to evaluate tissue damage.

Claims 13 is directed to the method of claim 2, wherein the cell condition is at least one of selected from the group consisting of cell viability, cell injury, molecular transport, and mitochondrial function. Ishimura et al. assess "injury to the cells (severity of cell necrosis) in the hepatic microcirculation" (page 5, lines 2-3). In addition, Ishimura et al. are concerned with the viability of graft preservation (page 4).

Accordingly, Ishimura et al. anticipated the instant claims.

Claims 1-16 are rejected under 35 U.S.C. 102(b) as being anticipated by Zikria et al (US-5,565,187, issued 15 October 1996).

Claim 1 is directed to a method of analyzing organ or tissue injury, comprising the following steps of: (a) labeling an organ or a tissue with dye; (b) obtaining multiple indices involving xenobiotic metabolism and/or cell condition of said organ or tissue; and (c) analyzing the organ or tissue injury from said indices. Zikria et al. teach "a method for evaluating the effect of trauma attributable to exposure to...toxic chemicals, carcinogens...on the capillary circulation of...fish fry or newly hatched amphibian tadpole...compris[ing] injecting into the yolk sac a fluorescent dye...and thereafter examining the capillary circulation...for signs of altered capillary circulation attributable to said trauma" (col.6, lines 35-49). Zikria et al. further teach, "method for evaluating potential anti-inflammatory drugs which comprises...introducing a drug believed to possess anti-inflammatory activity, exposing said salmonid, other teleost or amphibian to an inflammation inducing trauma, and thereafter examining the capillary circulation of said salmonid, other teleost or amphibian utilizing fluorescence microscopy for signs of altered capillary circulation." (col. 8, lines 12-24).

Claim 2 is directed to method of claim 1, wherein the organ or tissue is at least one selected from the group consisting of liver, kidney, lung, pancreas and

gastrointestinal tracts. Zikria et al. teach that fish models are used to study metabolism, pharmacology, physiology, and toxicology (col.2, lines 24-26) as well as "fish have been studied relative to environmental pollution and toxicology" (col.2, lines 30-32) and further indicate that recently published articles utilizing fish for such studies include a publication entitled, *Development of Cancer of the Liver After injection of Trout Eggs with Known Carcinogens* by Zikria et al. This suggests application of their method to liver.

Claim 3 is directed the method of claim 1, where the step (b) further comprises a step of obtaining microanatomical orientation of vascular system and/or excretion pathways. Zikria et al. describe orientation of the circulatory system after injection of the fluorescent molecules (col.1, lines 45-51).

Claim 4 is directed to the method of claim 1, wherein the analysis is carried out visually and/or quantitatively. Zikria et al. teach, "the capillary circulation...is examined utilizing fluorescence microscopy" (col.7, lines 18-21).

Claim 5 is directed to the method of claim 1, wherein the cell condition is at least one selected from the group consisting of cell viability, cell injury, molecular transport, and mitochondrial function. Zikria et al. teach, "method of identifying and quantifying increased vascular permeability" (col.3, lines 61-62) associated with cell injury (col.4, line 1).

Claim 6 is directed to a method of evaluating drug toxicity, comprising the following steps of: (a) labeling an organ or a tissue with dye; (b) applying a test drug to said organ or tissue; (c) obtaining multiple indices involving xenobiotic metabolism

and/or cell condition of said organ or tissue; (d) analyzing the organ or tissue injury from said indices; and (e) evaluating whether or not the drug have a toxicity to said organ or tissue. Zikria et al. teach "a method for evaluating the effect of trauma attributable to exposure to...toxic chemicals, carcinogens...on the capillary circulation of...fish fry or newly hatched amphibian tadpole...compris[ing] injecting into the yolk sac a fluorescent dye...and thereafter examining the capillary circulation...for signs of altered capillary circulation attributable to said trauma" (col.6, lines 35-49). Zikria et al. further teach, "method for evaluating potential anti-inflammatory drugs which comprises...introducing a drug believed to possess anti-inflammatory activity, exposing said salmonid, other teleost or amphibian to an inflammation inducing trauma, and thereafter examining the capillary circulation of said salmonid, other teleost or amphibian utilizing fluorescence microscopy for signs of altered capillary circulation." (col. 8, lines 12-24).

Claim 7 is directed to method of claim 6, wherein the organ or tissue is at least one selected from the group consisting of liver, kidney, lung, pancreas and gastrointestinal tracts. Zikria et al. teach that fish models are used to study metabolism, pharmacology, physiology, and toxicology (col.2, lines 24-26) as well as "fish have been studied relative to environmental pollution and toxicology" (col.2, lines 30-32) and further indicate that recently published articles utilizing fish for such studies include a publication entitled, *Development of Cancer of the Liver After injection of Trout Eggs with Known Carcinogens* by Zikria et al. This suggests their method can be applied to liver.

Claim 8 is directed to the method of claim 6, where the step (b) further comprises a step of obtaining microanatomical orientation of vascular system and/or excretion pathways. Zikria et al. describe orientation of the circulatory system after injection of the fluorescent molecules (col.1, lines 45-51).

Claim 9 is directed to the method of claim 6, wherein the analysis is carried out visually and/or quantitatively. Zikria et al. teach, "the capillary circulation...is examined utilizing fluorescence microscopy" (col.7, lines 18-21).

Claim 10 is directed to method of claim 6, wherein the cell condition is at least one selected from the group consisting of cell viability, cell injury, transport of molecules in and around cells, and generation of biologically active compounds, blood flow, and tissue oxygenation. Zikria et al. teach, "method of identifying and quantifying increased vascular permeability" (col.3, lines 61-62).

Claim 11 is directed the method of claim 2, where the step (b) further comprises a step of obtaining microanatomical orientation of vascular system and/or excretion pathways. Zikria et al. describe orientation of the circulatory system after injection of the fluorescent molecules (col.1, lines 45-51).

Claim 12 is directed to the method of claim 2, wherein the analysis is carried out visually and/or quantitatively. Zikria et al. teach, "the capillary circulation...is examined utilizing fluorescence microscopy" (col.7, lines 18-21).

Claims 13 is directed to the method of claim 2, wherein the cell condition is at least one of selected from the group consisting of cell viability, cell injury, molecular transport, and mitochondrial function. Zikria et al. teach, "method of identifying and

quantifying increased vascular permeability" (col.3, lines 61-62) associated with cell injury (col.4, line 1).

Claim 14 is directed the method of claim 7, where the step (b) further comprises a step of obtaining microanatomical orientation of vascular system and/or excretion pathways. Zikria et al. describe orientation of the circulatory system after injection of the fluorescent molecules (col.1, lines 45-51).

Claim 15 is directed to the method of claim 7, wherein the analysis is carried out visually and/or quantitatively. Zikria et al. teach, "the capillary circulation...is examined utilizing fluorescence microscopy" (col.7, lines 18-21).

Claims 16 is directed to the method of claim 7, wherein the cell condition is at least one of selected from the group consisting of cell viability, cell injury, molecular transport, and mitochondrial function. Zikria et al. teach, "method of identifying and quantifying increased vascular permeability" (col.3, lines 61-62) associated with cell injury (col.4, line 1).

Accordingly, Zikria et al. anticipated the instant claims.

Conclusion

No claims are allowed.

Examiner Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Scott Long** whose telephone number is **571-272-9048**. The examiner can normally be reached on Monday - Friday, 9am - 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Joseph Woitach** can be reached on **571-272-0739**. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Scott Long
Patent Examiner
Art Unit 1633

/Janet L. Epps-Ford/
Primary Examiner
Art Unit 1633

JLE